

PATENT COOPERATION TREATY

EXPRESS MAIL MAILING LABEL
NO.: EV631056332 45

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2004/001211

International filing date (day/month/year)
19.03.2004

Priority date (day/month/year)
19.03.2003

International Patent Classification (IPC) or both national classification and IPC
C12Q1/68, C12N15/10

Applicant
DISCERNA LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office - Glitschiner Str. 103
D-10958 Berlin
Tel. +49 30 25901 - 0
Fax: +49 30 25901 - 640

Authorized Officer

Schönwasser, D

Telephone No. +49 30 25901-318



10/549778

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**International application No.
PCT/GB2004/001211

JC05 Rec'd PCT/PTO 19 SEP 2005

Box No. 1 Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing:
 - ☒ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☒ furnished subsequently to this Authority for the purposes of search.
3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**International application No.
PCT/GB2004/001211**Box No. II Priority**1. ☒ The following document has not been furnished:☒ copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).☐ translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**International application No.
PCT/GB2004/001211**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 1-3, 7,8 (partially)

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☒ the claims, or said claims Nos. 1-3, 7,8 (partially) are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 1-3, 7,8 (partially)
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- | | |
|----------------------------|--|
| the written form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**International application No.
PCT/GB2004/001211**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
Industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Yes: Claims	19-32
	No: Claims	1-18
Inventive step (IS)	Yes: Claims	19-32
	No: Claims	1-18
Industrial applicability (IA)	Yes: Claims	1-32
	No: Claims	-

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/GB2004/001211**Re Item III.**

Present claims 1-3, 7 and 8 relate to an extremely large number of possible primers (see definition of primers on p. 4, l. 31-p.5, l. 31; p. 8, l. 1-22, which comprise basically ANY possible primer sequence). Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the primers claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to primers as defined by SEQ ID NO:1 and 3.

Re Item V.

The following documents are referred to in this communication:

- D1 : US6291170 (Stanford University (US)) 18 September 2001 (2001-09-18)
D2 : EP 0 549 107 A (SYNTEX INC) 30 June 1993 (1993-06-30)

1. Novelty and Inventive step (Art. 33(2)(3), PCT)

- 1.1 It is pointed out that the present opinion concerning novelty, inventive step and industrial applicability only refers to subject-matter for which an International Search Report has been established (see Item III).
- 1.2 The present application relates to primers used in single primer RT PCR, which comprise at their 5' end a sequence found in the 5' end of the RNA molecule to be transcribed ("5' consensus sequence") and which comprise at their 3' end a sequence which can hybridise to the 3' end of the 3' region of the RNA molecule to be transcribed ("hybridising sequence"). Methods for recovering cDNA, pref. in combination with ribosomal display, and kits for carrying out said methods are also claimed.
- 1.3 D1 discloses *inter alia* primers for RT-PCR, which comprise a "5' consensus sequence" (here: T7 RNA polymerase binding site) and a "hybridising sequence"

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/GB2004/001211

(here: poly T) (col. 3, lines 59-62; col. 8, lines 4-60; Fig. 1, SEQ ID NO:1). Further, a method for recovery of cDNA using said primer as the only primer (single primer PCR) in a reverse transcription step (col 3, lines 10-15) as well as a combination of this method with the use of a single primer, comprising the "5' consensus sequence" in a PCR reaction (SEQ ID NO:2) is described (col. 2, lines 14-19). Consequently, subject-matter of present claims 1-18 lacks novelty over D1 (Art. 33(2), PCT).

- 1.4 D2 describes several methods of single primer PCR, including a method which uses a primer containing a "5' consensus sequence" (here named EP2) and a "hybridising sequence" (here named EP1). The target polynucleotide to be amplified can be an RNA molecule which is amplified by the use of reverse transcriptase (Fig. 4; page 5, line 12-page 6, line 14; page 11, lines 47-49; page 15, lines 4-8; page 16, lines 44-45;).
In view of D2, subject-matter of claims 1-8 and 12-18 does not fulfil the requirement of novelty as set out in Art. 33(2), PCT.

Re Item VIII.

2. Clarity (Art. 6, PCT)

- 2.1 It is clear from the description and claims that it is essential for the primers used in all claimed cDNA recovery methods to comprise a 3' end as defined in claim 1 (i.e. "a 3' sequence capable of hybridising to a 3' region of the mRNA").
Since independent claims 12 and 22 do not contain this feature, said claims do not meet the requirement following from Article 6 PCT taken in combination with Rule 6.3(b) PCT that any independent claim must contain all the technical features essential to the definition of the invention.
- 2.2 It is not clear to which claim category (i.e. "product claim" or "method claim") claims 27 and 28 belong to.
- 2.3 Present claim 6 seems to be redundant in view of claims 1 and 5.